Inventor Search

=> d ibib abs ind l6 1-1

L6 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:533640 HCAPLUS
DOCUMENT NUMBER: 141:52868
TITLE: Passive immunization against Clostridium difficile disease
INVENTOR(S): **Thomas, William D.; Giannasca, Paul J.; Zhang, Zhenxi; Lei, Wende ; Monath, Thomas P.**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U.S. Ser. No. 815,452.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004126383	A1	20040701	US 2003-737270	20031216
US 6214341	B1	20010410	US 1998-176076	19981020
US 2001051153	A1	20011213	US 2001-815452	20010322
US 6680168	B2	20040120		

PRIORITY APPLN. INFO.:
US 1997-62522P P 19971020
US 1998-176076 A1 19981020
US 2001-815452 A2 20010322

AB The invention provides active and passive immunization methods for preventing and treating Clostridium difficile infection, which involve percutaneous administration of C. difficile toxin-neutralizing polyclonal immune globulin, C. difficile toxoids, or combinations thereof. Also provided by the invention are C. difficile toxoids, C. difficile toxin-neutralizing polyclonal immune globulin, and methods of identifying subjects that produce C. difficile toxin-neutralizing polyclonal immune globulin.

IC ICM A61K039-00
ICS A61K039-38
NCL 424184100
CC 15-3 (Immunochemistry)
Section cross-reference(s): 1, 63
ST passive immunization antibody polyclonal Ig Clostridium difficile infection; toxoid vaccine Clostridium difficile passive immunization bacterial infection
IT Diarrhea
(Clostridium difficile-associated; passive immunization against Clostridium difficile disease)
IT Infection
(bacterial; passive immunization against Clostridium difficile disease)
IT Drug delivery systems
(injections, i.m.; passive immunization against Clostridium difficile disease)
IT Drug delivery systems
(injections, i.v.; passive immunization against Clostridium difficile disease)
IT Drug delivery systems
(injections, s.c.; passive immunization against Clostridium difficile disease)
IT Clostridium difficile
Human

Vaccines
(passive immunization against Clostridium difficile disease)

IT Toxoids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(passive immunization against Clostridium difficile disease)

IT Immunization
(passive; passive immunization against Clostridium difficile disease)

IT Drug delivery systems
(percutaneous; passive immunization against Clostridium difficile disease)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(toxin-neutralizing, raised against a Clostridium difficile toxin or toxoid; passive immunization against Clostridium difficile disease)

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=> d que stat l31
L8          1825 SEA FILE=HCAPLUS ABB=ON  ?CLOSTRIDIUM?(W)?DIFFICILE?
L10            3 SEA FILE=HCAPLUS ABB=ON  L8 AND ?IMMUNE?(W)?GLOB?
L11          519 SEA FILE=HCAPLUS ABB=ON  L8 AND (?CLOSTRID?(W)(?TOXIN? OR
                 ?TOXOID?) OR ?TOXOID?)
L12          104 SEA FILE=HCAPLUS ABB=ON  L11 AND ?ANTIBOD?
L13            2 SEA FILE=HCAPLUS ABB=ON  L12 AND ?RECURR?(4A)?DIARRHEA?
L14            9 SEA FILE=HCAPLUS ABB=ON  L8 AND ?RECURR?(4A)?DIARRHEA?
L15           12 SEA FILE=HCAPLUS ABB=ON  L10 OR L13 OR L14
L16            3 SEA FILE=HCAPLUS ABB=ON  L15 AND ?RISK?
L17            5 SEA FILE=HCAPLUS ABB=ON  L15 AND (?DRUG?(W)(?DELIV? OR
                 ?ADMIN?) OR ?IMMUNIZ? OR ?VACCIN?)
L18          135 SEA FILE=HCAPLUS ABB=ON  L8 AND (?DRUG?(W)(?DELIV? OR ?ADMIN?)
                 OR ?IMMUNIZ? OR ?VACCIN?)
L19           10 SEA FILE=HCAPLUS ABB=ON  L18 AND ?RISK?
L20           21 SEA FILE=HCAPLUS ABB=ON  L15 OR L16 OR L17 OR L19
L21           12 SEA FILE=HCAPLUS ABB=ON  L20 AND ?HUMAN?
L22            8 SEA FILE=HCAPLUS ABB=ON  L20 AND ?METHOD?
L23           13 SEA FILE=HCAPLUS ABB=ON  L21 OR L22
L31            8 SEA FILE=HCAPLUS ABB=ON  L23 AND (PD<20010322 OR PRD<20010322)

=> d ibib abs l31 1-8

L31  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:533640  HCAPLUS
DOCUMENT NUMBER:          141:52868
TITLE:                    Passive immunization against
                          Clostridium difficile disease
INVENTOR(S):              Thomas, William D.; Giannasca, Paul J.; Zhang, Zhenxi;
                          Lei, Wende; Monath, Thomas P.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U.S.
                          Ser. No. 815,452.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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     US 2004126383         A1    20040701    US 2003-737270           20031216 <--
     US 6214341            B1    20010410    US 1998-176076           19981020 <--
     US 2001051153         A1    20011213    US 2001-815452           20010322 <--
     US 6680168            B2    20040120
PRIORITY APPLN. INFO.:                       US 1997-62522P      P    19971020 <--
                                             US 1998-176076      A1   19981020 <--
                                             US 2001-815452      A2   20010322
AB   The invention provides active and passive immunization
     methods for preventing and treating Clostridium
     difficile infection, which involve percutaneous administration of
     C. difficile toxin-neutralizing polyclonal immune
     globulin, C. difficile toxoids, or combinations thereof.  Also
     provided by the invention are C. difficile toxoids, C. difficile
     toxin-neutralizing polyclonal immune globulin, and
     methods of identifying subjects that produce C. difficile
     toxin-neutralizing polyclonal immune globulin.

L31  ANSWER 2 OF 8  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2002:46761  HCAPLUS
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DOCUMENT NUMBER: 136:385354
TITLE: Bovine hyperimmune whey protein concentrate with specific biological activity as a replacement ingredient
AUTHOR(S): Thorig, L.; de Groot, N.; Hensgens, C. M. H.
CORPORATE SOURCE: Muco Vax BV, Leiden, 2333 CA, Neth.
SOURCE: Innovations in Food Technology (**2001**), 13, 57-60
CODEN: INFTFU; ISSN: 1465-0460
PUBLISHER: Print Workshop Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. A preparation from natural bovine hyperimmune whey made by the Dutch biotechnol. company MucoVax is presented. The preparation contains specific Ig against **Clostridium difficile** and its toxins and can be used as a replacement ingredient in nutritional supplements, in functional foods, and in clin. nutrition. The use of anti-C. difficile hyperimmune whey protein concentrate could prevent the occurrence and/or decrease the **risk** of **recurrence** of C. difficile-associated **diarrhea** (CDAD). The whey preparation has high biol. value for uses in new products or product line extensions for clin. nutrition or dietary supplementation and can be effective in nutritional therapy of CDAD in **humans.** The high biol. value of the whey preparation allows its use at lower concns. in functional foods, thus decreasing possible **risk.** The preparation can be combined with micronutrients, antioxidants, insol. dietary fiber, prebiotics, and probiotics for preventive nutritional support to increase the protection in elderly **humans** in rehabilitation/geriatric wards against the outbreaks of CDAD.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:594901 HCAPLUS
DOCUMENT NUMBER: 131:219184
TITLE: Colonic delivery of protein or peptide compositions
INVENTOR(S): Luck, Michael S.; Crabb, Joseph H.
PATENT ASSIGNEE(S): Immucell Corporation, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945903	A1	19990916	WO 1999-US4366	19990226 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6074689	A	20000613	US 1998-37647	19980310 <--
CA 2323062	AA	19990916	CA 1999-2323062	19990226 <--
AU 9929758	A1	19990927	AU 1999-29758	19990226 <--
EP 1061902	A1	20001227	EP 1999-911014	19990226 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 2002506018 T2 20020226 JP 2000-535318 19990226 <--

PRIORITY APPLN. INFO.: US 1998-37647 A 19980310 <--
WO 1999-US4366 W 19990226 <--

AB A **method** for delivering an active protein (preferably an Ig) or a peptide to the colon and a coated multiparticulate dosage composition for orally delivering an active protein or peptide to the colon produced by the **method** comprises (a) providing an aqueous PEG solution; (b) providing a dry, homogeneous mixture of the active protein or peptide and microcryst. cellulose; (c) spraying said aqueous PEG solution onto said homogeneous mixture; (d) extruding; (e) spheronizing the extrudate; (f) drying; (g) screening the dried composition to form multiparticulates; (h) collecting and subsequently coating said multiparticulates. Multiparticulates containing **Clostridium difficile** toxin A and B **hyperimmune globulin** were prepared according to above procedure and were coated with an entro-colonic coating comprising methocel E5 and Eudragit S100. The entro-colonic coated multiparticulate formulation prevented gastric acid degradation of the Ig specific activity and released only 15% of the total activity at pH representative of the proximal intestine (pH = 6.0) and 80% of the total activity at a pH representative of the distal ileum and colon (pH = 7.0).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:425504 HCAPLUS
DOCUMENT NUMBER: 131:72729
TITLE: **Vaccine** for Clostridium botulinum neurotoxin
INVENTOR(S): Williams, James A.
PATENT ASSIGNEE(S): Ophidian Pharmaceuticals, Inc., USA
SOURCE: U.S., 140 pp., Cont.-in-part of U.S. Ser. No. 329,154, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5919665	A	19990706	US 1995-405496	19950316 <--
US 5196193	A	19930323	US 1989-429791	19891031 <--
US 5601823	A	19970211	US 1993-161907	19931202 <--
US 5599539	A	19970204	US 1994-255009	19940607 <--
US 5443976	A	19950822	US 1994-275304	19940714 <--
US 6613326	B1	20030902	US 1994-305411	19940913 <--
US 5904922	A	19990518	US 1995-442000	19950516 <--
US 5736139	A	19980407	US 1995-480604	19950607 <--
CA 2203504	AA	19960502	CA 1995-2203504	19951023 <--
CA 2416318	AA	19960502	CA 1995-2416318	19951023 <--
WO 9612802	A1	19960502	WO 1995-US13737	19951023 <--
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9539683	A1	19960515	AU 1995-39683	19951023 <--

AU 709586	B2	19990902			
EP 796326	A1	19970924	EP 1995-937626	19951023	<--
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BR 9509903	A	19971125	BR 1995-9903	19951023	<--
CN 1176658	A	19980318	CN 1995-196424	19951023	<--
HU 78048	A2	19990728	HU 1999-1238	19951023	<--
EP 1041149	A2	20001004	EP 2000-105371	19951023	<--
EP 1041149	A3	20010502			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV					
JP 2002514886	T2	20020521	JP 1996-514127	19951023	<--
NZ 337543	A	20020628	NZ 1995-337543	19951023	<--
JP 2003137897	A2	20030514	JP 2002-238940	19951023	<--
ZA 9508990	A	19960515	ZA 1995-8990	19951024	<--
US 6656468	B1	20031202	US 1997-810908	19970305	<--
FI 9701732	A	19970623	FI 1997-1732	19970423	<--
NO 9701868	A	19970624	NO 1997-1868	19970423	<--
US 6290960	B1	20010918	US 1997-915136	19970820	<--
US 6613329	B1	20030902	US 1998-84517	19980526	<--
AU 9948763	A1	19991125	AU 1999-48763	19990916	<--
AU 747841	B2	20020523			
AU 758820	B2	20030403	AU 1999-63043	19991202	<--
AU 9963043	A1	20000511			
US 2003219457	A1	20031127	US 2002-271012	20021015	<--
US 2003215468	A1	20031120	US 2003-354774	20030130	<--
US 2004062771	A1	20040401	US 2003-662918	20030915	<--
US 2004115215	A1	20040617	US 2003-729122	20031205	<--
US 2004142455	A1	20040722	US 2003-729039	20031205	<--
PRIORITY APPLN. INFO.:			US 1989-429791	A2 19891031	<--
			US 1992-985321	A2 19921204	<--
			US 1993-161907	A2 19931202	<--
			US 1994-329154	B2 19941024	<--
			US 1992-842709	A2 19920226	<--
			US 1992-983668	B1 19921201	<--
			US 1993-147009	B1 19931102	<--
			US 1994-275304	A3 19940714	<--
			US 1995-405496	A2 19950316	<--
			US 1995-422711	A2 19950414	<--
			US 1995-456997	B1 19950601	<--
			US 1995-480604	A 19950607	<--
			AU 1995-39683	A3 19951023	<--
			CA 1995-2203504	A3 19951023	<--
			EP 1995-937626	A3 19951023	<--
			JP 1996-514127	A3 19951023	<--
			WO 1995-US13737	W 19951023	<--
			US 1996-704159	A1 19960828	<--
			US 1997-810908	A1 19970305	<--
			US 2002-271012	A3 20021015	

AB The present invention includes recombinant proteins derived from toxins of Clostridium botulinum and **Clostridium difficile.** In particular, soluble recombinant fusion proteins comprising Clostridium botulinum type A toxin proteins are provided. **Methods** which allow for the isolation of recombinant proteins free of significant endotoxin contamination are provided. The soluble, endotoxin-free recombinant proteins are used as immunogens for the production of **vaccines** and antitoxins. These **vaccines** and antitoxins are useful in the treatment of **humans** and other animals at **risk** of intoxication with clostridial toxin.

REFERENCE COUNT: 117 THERE ARE 117 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L31 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:644664 HCAPLUS
DOCUMENT NUMBER: 130:50959
TITLE: Prospects for a **vaccine** for **Clostridium difficile**
AUTHOR(S): Kyne, Lorraine; Kelly, Ciaran P.
CORPORATE SOURCE: Division of Gerontology, Beth Israel Deaconess Medical Center, Boston, MA, USA
SOURCE: BioDrugs (**1998**), 10(3), 173-181
CODEN: BIDRF4; ISSN: 1173-8804
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review withy 71 refs. C. difficile diarrhea and colitis is a new disease that is attributable to broad spectrum antibiotic therapy. During the past 2 decades C. difficile has become one of the most common nosocomial pathogens in the developed world. Disease caused by this organism is caused by the inflammatory actions of its 2 toxins, A and B, on the intestinal mucosa. **Human** antibody responses to these toxins are common in the general population and in patients with C. difficile-associated disease. There is evidence to indicate that antitoxin antibodies provide protection against severe, prolonged, or **recurrent** C. difficile **diarrhea.** Immunity induced by oral or parenteral passive administration of antibody is protective in animal models of C. difficile infection. In **humans**, i.v. passive **immunization** with pooled **human** Ig has been successful in the treatment of recurrent and severe C. difficile colitis. **Human** trials of oral passive immunotherapy with bovine Ig therapy are in progress. Formalin-inactivated culture filtrate from toxigenic C. difficile, as well as purified and inactivated toxins, have been used to successfully **immunize** animals. Similar prepns. are under investigation as possible **human vaccines.** Active **immunization** is probably the most promising approach to long term control of this difficult iatrogenic disease.
REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:226712 HCAPLUS
DOCUMENT NUMBER: 128:299540
TITLE: Treatment of **Clostridium difficile** -induced disease
INVENTOR(S): Kink, John A.; Thalley, Bruce S.; Stafford, Douglas C.; Firca, Joseph R.; Padhye, Nisha V.
PATENT ASSIGNEE(S): Ochidian Pharmaceuticals, Inc., USA
SOURCE: U.S., 205 pp., Cont.-in-part of U.S. Ser. No. 422,711.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5736139	A	19980407	US 1995-480604	19950607 <--
US 5196193	A	19930323	US 1989-429791	19891031 <--
US 5601823	A	19970211	US 1993-161907	19931202 <--
US 5599539	A	19970204	US 1994-255009	19940607 <--

US 5443976	A	19950822	US 1994-275304	19940714	<--
US 6613326	B1	20030902	US 1994-305411	19940913	<--
US 5919665	A	19990706	US 1995-405496	19950316	<--
US 5904922	A	19990518	US 1995-442000	19950516	<--
CA 2203504	AA	19960502	CA 1995-2203504	19951023	<--
CA 2416318	AA	19960502	CA 1995-2416318	19951023	<--
WO 9612802	A1	19960502	WO 1995-US13737	19951023	<--
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RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9539683	A1	19960515	AU 1995-39683	19951023	<--
AU 709586	B2	19990902			
EP 796326	A1	19970924	EP 1995-937626	19951023	<--
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BR 9509903	A	19971125	BR 1995-9903	19951023	<--
CN 1176658	A	19980318	CN 1995-196424	19951023	<--
HU 78048	A2	19990728	HU 1999-1238	19951023	<--
EP 1041149	A2	20001004	EP 2000-105371	19951023	<--
EP 1041149	A3	20010502			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV					
JP 2002514886	T2	20020521	JP 1996-514127	19951023	<--
NZ 337543	A	20020628	NZ 1995-337543	19951023	<--
JP 2003137897	A2	20030514	JP 2002-238940	19951023	<--
ZA 9508990	A	19960515	ZA 1995-8990	19951024	<--
US 6656468	B1	20031202	US 1997-810908	19970305	<--
FI 9701732	A	19970623	FI 1997-1732	19970423	<--
NO 9701868	A	19970624	NO 1997-1868	19970423	<--
US 6290960	B1	20010918	US 1997-915136	19970820	<--
AU 9948763	A1	19991125	AU 1999-48763	19990916	<--
AU 747841	B2	20020523			
AU 758820	B2	20030403	AU 1999-63043	19991202	<--
AU 9963043	A1	20000511			
US 2004062771	A1	20040401	US 2003-662918	20030915	<--

PRIORITY APPLN. INFO.:	US 1989-429791	A2	19891031 <--
	US 1992-985321	A2	19921204 <--
	US 1993-161907	A2	19931202 <--
	US 1994-329154	A2	19941024 <--
	US 1995-405496	A2	19950316 <--
	US 1995-422711	A2	19950414 <--
	US 1992-842709	A2	19920226 <--
	US 1992-983668	B1	19921201 <--
	US 1993-147009	B1	19931102 <--
	US 1994-275304	A3	19940714 <--
	US 1995-456997	B1	19950601 <--
	US 1995-480604	A	19950607 <--
	AU 1995-39683	A3	19951023 <--
	CA 1995-2203504	A3	19951023 <--
	EP 1995-937626	A3	19951023 <--
	JP 1996-514127	A3	19951023 <--
	WO 1995-US13737	W	19951023 <--
	US 1997-810908	A1	19970305 <--

AB The present provides neutralizing antitoxin directed against C. difficile toxins. These antitoxins are produced in avian species using soluble recombinant C. difficile toxin proteins. The avian antitoxins are designed so as to be orally administrable in therapeutic amts. and may be

in any form (i.e., as a solid or in aqueous solution). Solid forms of the antitoxin may comprise an enteric coating. These antitoxins are useful in the treatment of **humans** and other animals intoxicated with at least one bacterial toxin. The invention further provides **vaccines** capable of protecting a **vaccinated** recipient from the morbidity and mortality associated with C. difficile infection. These **vaccines** are useful for administration to **humans** and other animals at **risk** of exposure to C. difficile toxins.

REFERENCE COUNT: 99 THERE ARE 99 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:163478 HCAPLUS
DOCUMENT NUMBER: 128:242882
TITLE: Multivalent **vaccine** for Clostridium botulinum neurotoxin
INVENTOR(S): Williams, James A.; Thalley, Bruce S.
PATENT ASSIGNEE(S): Ophidian Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 428 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808540	A1	19980305	WO 1997-US15394	19970828 <--
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9742450	A1	19980319	AU 1997-42450	19970828 <--
EP 1105153	A1	20010613	EP 1997-940746	19970828 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AU 758820	B2	20030403	AU 1999-63043	19991202 <--
AU 9963043	A1	20000511		

PRIORITY APPLN. INFO.:			
US 1996-704159	A	19960828 <--	
AU 1995-39683	A	19951023 <--	
WO 1997-US15394	W	19970828 <--	

AB The present invention includes recombinant proteins derived from Clostridium botulinum toxins. In particular, soluble recombinant Clostridium botulinum type A, type B and type E toxin proteins are provided. **Methods** which allow for the isolation of recombinant proteins free of significant endotoxin contamination are provided. The soluble, endotoxin-free recombinant proteins are used as immunogens for the production of **vaccines** and antitoxins. These **vaccines** and antitoxins are useful in the treatment of **humans** and other animals at **risk** of intoxication with clostridial toxin. Thus, recombinant C. difficile toxin A and B gene and proteins and C. botulinum type A.apprx.G neurotoxin gene and proteins were prepared as **vaccines.**

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:265611 HCAPLUS
DOCUMENT NUMBER: 126:250218
TITLE: **Methods** and compositions for prevention and treatment of **Clostridium difficile** -associated diseases

INVENTOR(S): Gerding, Dale N.
PATENT ASSIGNEE(S): Gerding, Dale N., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9709886	A1	19970320	WO 1996-US14868		19960913	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG						
AU 9673620	A1	19970401	AU 1996-73620		19960913	<--
EP 952773	A1	19991103	EP 1996-935833		19960913	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI						
CA 2232001	C	20021210	CA 1996-2232001		19960913	<--
US 6635260	B1	20031021	US 1999-386464		19990809	<--
PRIORITY APPLN. INFO.:			US 1995-3847P	P	19950915	<--
			WO 1996-US14868	W	19960913	<--

AB The invention provides **methods** and compns. for preventing and treating **Clostridium difficile**-associated disease in a subject, wherein the subject is either a **human** or a non-**human** animal. The composition is especially useful for preventing **risk** of **Clostridium difficile**-associated disease caused by antimicrobials or antineoplastics in **human** or animal or birds. The **method** comprises administering to the subject an effective amount of a non-toxigenic strain of C. difficile or a combination of strains. A suitable non-toxigenic strain is selected from the M, T, C, P, S and Ap group as defined by restriction endonuclease anal. of pattern on agarose gel. Also provided are pharmaceutical compns. and unit dosage forms comprising a single strain or a combination of strains selected from a non-toxigenic. C. difficile group and a **method** for selecting non-toxigenic C. difficile strains.

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=> d que stat l30
L8          1825 SEA FILE=HCAPLUS ABB=ON  ?CLOSTRIDIUM?(W)?DIFFICILE?
L10            3 SEA FILE=HCAPLUS ABB=ON  L8 AND ?IMMUNE?(W)?GLOB?
L11          519 SEA FILE=HCAPLUS ABB=ON  L8 AND (?CLOSTRID?(W)(?TOXIN? OR
                 ?TOXOID?) OR ?TOXOID?)
L12          104 SEA FILE=HCAPLUS ABB=ON  L11 AND ?ANTIBOD?
L13            2 SEA FILE=HCAPLUS ABB=ON  L12 AND ?RECURR?(4A)?DIARRHEA?
L14            9 SEA FILE=HCAPLUS ABB=ON  L8 AND ?RECURR?(4A)?DIARRHEA?
L15           12 SEA FILE=HCAPLUS ABB=ON  L10 OR L13 OR L14
L16            3 SEA FILE=HCAPLUS ABB=ON  L15 AND ?RISK?
L17            5 SEA FILE=HCAPLUS ABB=ON  L15 AND (?DRUG?(W)(?DELIV? OR
                 ?ADMIN?) OR ?IMMUNIZ? OR ?VACCIN?)
L18          135 SEA FILE=HCAPLUS ABB=ON  L8 AND (?DRUG?(W)(?DELIV? OR ?ADMIN?)
                 OR ?IMMUNIZ? OR ?VACCIN?)
L19           10 SEA FILE=HCAPLUS ABB=ON  L18 AND ?RISK?
L20           21 SEA FILE=HCAPLUS ABB=ON  L15 OR L16 OR L17 OR L19
L21           12 SEA FILE=HCAPLUS ABB=ON  L20 AND ?HUMAN?
L22            8 SEA FILE=HCAPLUS ABB=ON  L20 AND ?METHOD?
L23           13 SEA FILE=HCAPLUS ABB=ON  L21 OR L22
L24          244 SEA L23
L25          193 DUP REMOV L24 (51 DUPLICATES REMOVED)
L28          152 SEA L25 AND DIARRHEA?
L29          149 SEA L28 AND HUMAN?
L30           26 SEA L29 AND METHOD?

 => d ibib abs l30 1-26

L30  ANSWER 1 OF 26     MEDLINE on STN
ACCESSION NUMBER:   2003314592     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 12843107
TITLE:              Molecular analysis of Clostridium
                    difficile strains isolated from 18 cases of
                    recurrent clostridium difficile
                    -associated diarrhea.
AUTHOR:             Tang-Feldman Yajarayma; Mayo Susan; Silva Jr Joseph Jr;
                    Cohen Stuart H
CORPORATE SOURCE:   Department of Internal Medicine, Division of Infectious and
                    Immunologic Diseases, University of California, Davis
                    Medical Center, Sacramento, California 95817, USA.
SOURCE:             Journal of clinical microbiology, (2003 Jul) 41 (7) 3413-4.
                    Journal code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200310
ENTRY DATE:         Entered STN: 20030708
                    Last Updated on STN: 20031003
                    Entered Medline: 20031002
AB   Recurrence of Clostridium difficile
     -associated diarrhea (CDAD) occurs in 15 to 20% of patients
     after discontinuation of treatment.  Arbitrarily primed PCR was used to
     investigate the epidemiology of recurrent CDAD in 18 patients.
     Reinfection with a new strain occurred in 6 of 18 patients (33.3%), while
     12 patients relapsed with the original strain shortly after
     discontinuation of treatment.  These data suggest that reinfection with
     exogenous C. difficile is a common problem and that not all recurrences
     are due to relapse.

L30  ANSWER 2 OF 26     MEDLINE on STN
```

ACCESSION NUMBER: 2001148109 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11159994
TITLE: Safety and immunogenicity of increasing doses of a **Clostridium difficile** toxoid **vaccine** administered to healthy adults.
AUTHOR: Kotloff K L; Wasserman S S; Losonsky G A; Thomas W Jr; Nichols R; Edelman R; Bridwell M; Monath T P
CORPORATE SOURCE: Division of Infectious Disease and Tropical Pediatrics, Department of Pediatrics, Center for Vaccine Development, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA.. kkotoff@medicine.umaryland.edu
CONTRACT NUMBER: NO1-AI-45251 (NIAID)
SOURCE: Infection and immunity, (2001 Feb) 69 (2) 988-95. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL) (CLINICAL TRIAL, PHASE I) Journal; Article; (JOURNAL ARTICLE) (RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010315

AB **Clostridium difficile** is a major cause of nosocomial **diarrhea** in industrialized countries. Although most illnesses respond to available therapy, infection can increase morbidity, prolong hospitalization, and produce life-threatening colitis. **Vaccines** are being explored as an alternative means for protecting high-**risk** individuals. We assessed the safety, immunogenicity, and dose response of a parenteral **vaccine** containing C. difficile toxoids A and B. Thirty healthy adults were assigned to receive four spaced inoculations on days 1, 8, 30, and 60 with one of three doses of **vaccine** (6.25, 25, or 100 microg). At each dose level, subjects were randomized, in a double-blind fashion, to receive either the soluble toxoids (n = 5) or toxoids adsorbed to alum (n = 5). Subjects were monitored for clinical and immunologic responses to **vaccination.** **Vaccination** was generally well tolerated, with occasional, usually mild, systemic reactions (abdominal pain, arthralgia, and **diarrhea**). The most common local reaction, mild arm pain, was reported by all recipients of the toxoid-alum formulation. Nearly all subjects (> or = 90%) developed vigorous serum antibody responses to both toxins, as measured by immunoglobulin G (IgG) enzyme-linked immunosorbent assay and neutralization of cytotoxicity, whereas fecal IgA increases occurred in approximately 50%. Statistically significant effects of dose and formulation on immunogenicity were not seen, although antibody levels tended to be higher with the alum-adjuvanted formulations and with increasing doses of soluble toxoid. Serum antibody responses among the toxoid-alum group appeared to plateau at 25 microg. We concluded that the C. difficile toxoid **vaccine** is safe and immunogenic in healthy volunteers. Further development as a prophylactic **vaccine** or for producing C. difficile **hyperimmune globulin** is justified.

L30 ANSWER 3 OF 26 MEDLINE on STN
ACCESSION NUMBER: 97268832 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9114180
TITLE: **Recurrent Clostridium difficile diarrhea**: characteristics of and **risk**

factors for patients enrolled in a prospective, randomized, double-blinded trial.
AUTHOR: Fekety R; McFarland L V; Surawicz C M; Greenberg R N; Elmer G W; Mulligan M E
CORPORATE SOURCE: Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor, USA.
SOURCE: Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, (1997 Mar) 24 (3) 324-33.
Journal code: 9203213. ISSN: 1058-4838.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970709
Last Updated on STN: 19970709
Entered Medline: 19970620

AB **Recurrent Clostridium difficile diarrhea** (RCDD) occurs in 20% of patients after they have received standard antibiotic treatment with vancomycin or metronidazole, but the reasons for the recurrences are largely unknown. Patients receiving vancomycin or metronidazole for active C. difficile **diarrhea** (CDD) were referred to our study centers for treatment and a 2-month follow-up as part of a randomized placebo-controlled trial. Sixty patients had RCDD (median number of episodes, 3.0; range, 2-9 episodes) and 64 were having their first episode of CDD. Patients with RCDD had more-severe abdominal pain and were more likely to have fever but initially responded well to antibiotic therapy. Data on sequential episodes showed no progression in disease severity. Five factors were associated with a higher **risk** of RCDD: the number of previous CDD episodes, onset of the initial disease in the spring, exposure to additional antibiotics for treatment of other infections, infection with immunoblot type 1 or 2 strains of C. difficile, and female gender. These factors may help to identify patients who are more likely to develop RCDD and require careful medical supervision.

L30 ANSWER 4 OF 26 MEDLINE on STN
ACCESSION NUMBER: 95119482 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7819650
TITLE: **Diarrhea** with enteral feeding: prospective reappraisal of putative causes.
AUTHOR: Heimburger D C; Sockwell D G; Geels W J
CORPORATE SOURCE: Department of Nutrition Sciences, University of Alabama at Birmingham.
CONTRACT NUMBER: CA-28103 (NCI)
CA-47888 (NCI)
SOURCE: Nutrition (Burbank, Los Angeles County, Calif.), (1994 Sep-Oct) 10 (5) 392-6.
Journal code: 8802712. ISSN: 0899-9007.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502

ENTRY DATE: Entered STN: 19950223
Last Updated on STN: 19950223
Entered Medline: 19950216

AB Our objective was to test, in tube-fed patients whether treatment with antibiotics, the presence of hypoalbuminemia, or the use of hypertonic tube feeding is associated with a higher incidence of **diarrhea**; how often tube feeding actually causes **diarrhea**; and whether administration of a Lactobacillus preparation reduces the incidence of **diarrhea**. Our study design included a randomized, double-blind, placebo-controlled trial of patients on tube feeding for at least 5 days. Stool weights and clinical assessment of bowel function were used as outcome measures. **Diarrhea** was defined as > 200 g of stool, or three or more liquid stools, in any 24-h period. The tube feeding was considered responsible for **diarrhea** only when the latter resolved on discontinuation of the feeding. When **diarrhea** did not resolve, other causes were sought. Of 62 patients enrolled, 41 reached a trial end point. Of these, 34 completed 5 days of feeding without **diarrhea**, and 7 experienced **diarrhea**.
Although **diarrhea** was associated with hypoalbuminemia and with protracted treatment with antibiotics, in only 1 subject who had a history of gastric surgery was it caused by tube feeding. The other 6 cases of **diarrhea** were caused by factors other than tube feeding, mainly **drugs administered** through the tube. Lactobacillus treatment did not alter the **risk** of **diarrhea**.
Diarrhea occurs more commonly in tube-fed patients who have low serum albumin levels and have been treated with antibiotics for long periods, but these associations are generally not causal. Hypertonic feeding formulas are not associated with increased **risk** of **diarrhea**. Most cases of **diarrhea** in tube-fed patients are caused by factors extraneous to the tube feeding.

L30 ANSWER 5 OF 26 MEDLINE on STN
ACCESSION NUMBER: 89086457 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2910090
TITLE: Treatment of antibiotic-associated **Clostridium difficile** colitis with oral vancomycin: comparison of two dosage regimens.
AUTHOR: Fekety R; Silva J; Kauffman C; Buggy B; Deery H G
CORPORATE SOURCE: Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor 48109-0378.
CONTRACT NUMBER: NIAID 21076 (NIAID)
SOURCE: American journal of medicine, (1989 Jan) 86 (1) 15-9.
Journal code: 0267200. ISSN: 0002-9343.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198902
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19950206
Entered Medline: 19890206

AB PURPOSE: High-dose (500 mg orally four times daily) vancomycin is considered by many investigators to be the most effective treatment for antibiotic-associated **Clostridium difficile** colitis.
However, a lower dosage of 125 or 150 mg given three or four times a day has become popular, has been shown to be effective, and is less expensive than the high-dose regimen. We therefore decided to compare two vancomycin dosage regimens in a randomized trial. PATIENTS AND

METHODS: The study involved 46 hospitalized patients with serious underlying diseases complicated by C. difficile **diarrhea** or colitis. Patients were assigned (according to a table of random numbers) to treatment with either 125 or 500 mg of vancomycin orally four times daily for an average of 10 days. RESULTS: No significant differences in measurable responses to the two regimens were noted. There were no treatment failures. The mean duration of **diarrhea** after initiation of therapy was about four days, and almost all patients had no **diarrhea** after one week. The organism continued to be demonstrated in the stools of about 50 percent of patients for the first few weeks after completion of therapy, and nine (20 percent) patients developed a **recurrence** of their **diarrheal** illness. Vancomycin was well tolerated by all patients. CONCLUSION: Since the dose of 125 mg appeared to be as effective as the 500-mg dose, which is more expensive, the 125-mg dose is preferred when vancomycin is used in treatment of this disease, unless the patient is critically ill.

L30 ANSWER 6 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2004:13603 BIOSIS
DOCUMENT NUMBER: PREV200400015718
TITLE: Intravenous immunoglobulin for the treatment of recurrent **Clostridium difficile** diarrhoea.
AUTHOR(S): Wilcox, M. H. [Reprint Author]
CORPORATE SOURCE: University of Leeds, Leeds, UK
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2003) Vol. 43, pp. 367. print. Meeting Info.: 43rd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, IL, USA. September 14-17, 2003. American Society for Microbiology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Dec 2003
Last Updated on STN: 24 Dec 2003

AB Background: Treatment of recurrent C. difficile diarrhoea (CDD) is a therapeutic challenge, and is complicated by the profound disruption of gut flora by repeated courses of antimicrobial therapy. Evidence linking impaired production of anti-toxin A antibody to recurrent CDD provides a rationale for intravenous (iv) immunoglobulin (IG) therapy in such cases. Reports of the effectiveness of this approach may be biased towards successfully treated cases. **Methods**: Patients receiving iv Ig for recurrent CDD in our hospital over the past 2 years were identified by review of Pharmacy and Microbiology databases. Patients records were reviewed to determine disease severity and response to treatment. Results: Of 580 CD cytotoxin positive patients, 5 received iv Ig because of protracted and/or recurrent CDD (median duration 50 days, range 45-64); 2 had biopsy proven pseudomembranous colitis. The 5 patients received a median 3 non-CDD antibiotic courses (range 2-8), all became hypoalbuminaemic (median 27 g/L, range 11-29; normal 37-49), 3 had marked hypokalaemia (range 1.9-2.7 mMol/L; normal 3.6-5), 3 had a markedly raised peripheral white cell count (18-34; normal 4-11X109/L), 3 had abdominal signs, and one was pyrexial. The 5 cases received metronidazole for median 17 days (range 0-63) plus vancomycin for median 14 days (range 10-42) before iv IG. One also received rifampicin plus vancomycin and one was given S. boulardii. Iv IG was given at a dosage of 300-500 mg/kg (most commonly 400 mg/kg) for 1 dose (2 patients), 2 doses (2 patients) and in 1 case for 6 doses. The latter patient died of intractable CDD, 3 had a good therapeutic response to iv IG, and CDD recurred within 6 weeks in 1 case. In the 3 successfully treated cases, CDD resolved within 11 days. Conclusions: Non-CDD antibiotic therapy must be avoided to prevent

CDD recurrence. Iv IG is useful for the treatment of intractable and severe CDD. In successfully treated cases, response is comparable with that seen for conventional antibiotic therapy. Other forms of passive immunotherapy should be explored.

L30 ANSWER 7 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:608293 BIOSIS
DOCUMENT NUMBER: PREV200200608293
TITLE: Bacteriophages of **Clostridium difficile**
AUTHOR(S): Goh, S. [Reprint author]; Chang, B. J. [Reprint author]; Riley, T. V. [Reprint author]
CORPORATE SOURCE: University of Western Australia, Crawley, WA, Australia
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2002) Vol. 102, pp. 301. print. Meeting Info.: 102nd General Meeting of the American Society for Microbiology. Salt Lake City, UT, USA. May 19-23, 2002. American Society for Microbiology. ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Nov 2002
Last Updated on STN: 27 Nov 2002

AB The anaerobe **Clostridium difficile** causes antibiotic-associated **diarrhea** and pseudomembranous colitis in hospital patients. Virulence of C. difficile is mediated in part via the production of toxins A and B. Antibiotic treatment of C. difficile-associated **diarrhea** often results in **recurrent** infection and may contribute to the development of antibiotic resistant bacteria, such as vancomycin-resistant enterococci. A possible role for phages as an alternative treatment along with their role in toxin production was investigated. No lytic phages were found, however four temperate dsDNA phages were isolated and characterized. Phages C2, C5 and C8 morphologically belong to Myoviridae, while C6 was a Siphoviridae phage. Their genome sizes ranged from 35-44kb. Other phage characteristics determined were burst size and latent periods, host range and buoyant densities. Phage DNA restriction enzyme digestion patterns generated by XbaI and HindIII suggested a close relationship between C2 and C5, while C8 displayed some similarity to C2 and C5. There was no similarity between C6 and the other phages. The production of toxins A and B by some lysogens was increased compared to uninfected strains and was host-dependent. PCR with primers for amplification of toxin genes and Southern hybridization experiments are underway in order to determine the role of the phages in toxin production.

L30 ANSWER 8 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:482741 BIOSIS
DOCUMENT NUMBER: PREV200000482741
TITLE: Relapse vs. reinfection in HIV-positive patients suffering from **recurrent Clostridium difficile**-associated **diarrhea** (CDAD) episodes: A molecular analysis.
AUTHOR(S): Alonso, R. [Reprint author]; Gros, S. [Reprint author]; Pelaez, T. [Reprint author]; Garcia De Viedma, D. [Reprint author]; Rodriguez Creixems, M. [Reprint author]; Bouza, E. [Reprint author]
CORPORATE SOURCE: Hosp. Gregorio Maranon, Madrid, Spain
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1999) Vol. 39, pp. 602. cd-rom.

Meeting Info.: 39th Interscience Conference on Antimicrobial Agents and Chemotherapy. San Francisco, California, USA. September 26-29, 1999. American Society for Microbiology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Nov 2000
Last Updated on STN: 10 Jan 2002

L30 ANSWER 9 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:480825 BIOSIS
DOCUMENT NUMBER: PREV200000480825
TITLE: Epidemiology of **recurrent Clostridium difficile**-associated **diarrhea** (CDAD).
AUTHOR(S): Mayo, S. [Reprint author]; Tang, Y. J. [Reprint author]; Silva, J. J. [Reprint author]; Cohen, S. H. [Reprint author]
CORPORATE SOURCE: Univ. of California, Davis, Sacramento, CA, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1999) Vol. 39, pp. 601. cd-rom. Meeting Info.: 39th Interscience Conference on Antimicrobial Agents and Chemotherapy. San Francisco, California, USA. September 26-29, 1999. American Society for Microbiology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Nov 2000
Last Updated on STN: 10 Jan 2002

L30 ANSWER 10 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004297116 EMBASE
TITLE: **Clostridium difficile** colitis.
AUTHOR: Lamont J.T.
CORPORATE SOURCE: Dr. J.T. Lamont, Division of Gastroenterology, Beth Israel Deaconess Medical Center, Harvard Medical School, 330 Brookline Avenue, Boston, MA 02215, United States. jlamont@bidmc.harvard.edu
SOURCE: European Surgery - Acta Chirurgica Austriaca, (2004) 36/3 (161-165).
Refs: 28
ISSN: 1682-1769 CODEN: ESUUBR
COUNTRY: Austria
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English; German
AB Background: **Clostridium difficile** is one of the most prevalent hospital pathogens known with an attack rate of 20-25 % in many American and European hospitals. **Methods**: Review of experimental and clinical data on C. difficile colitis. Results: The organism produces colitis and **diarrhea** by secreting two protein exotoxins into the lumen of the bowel. These toxins, called toxin A and toxin B, are not related to other known bacterial enterotoxins. They bind to cell surface

receptors on colonocytes, enter the cell, and then inactivate a family of signaling molecules that regulate the cytoskeleton. The resulting damage to the colonic epithelium leads eventually to secretion of water (**diarrhea**) and severe inflammation (pseudomembranous colitis), the two hallmarks of this infection. Recent discoveries of the critical role played by the host immune response to C. difficile should allow us to eventually control this infection by **vaccination.** Serum IgG antibodies to toxin A protect patients against the toxins by preventing their attachment to the epithelium of the large bowel. Approximately 70 % of healthy infants are carriers, that is, they are resistant to the effects of the toxin. Only later in life does infection with C. difficile lead to symptoms. Conclusions: This review will focus on the contributions of basic and clinical investigators to our understanding of this widespread pathogen and to ongoing efforts to control it.

L30 ANSWER 11 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003242860 EMBASE
TITLE: Adverse drug event trigger tool: A practical **methodology** for measuring medication related harm.
AUTHOR: Rozich J.D.; Haraden C.R.; Resar R.K.
CORPORATE SOURCE: Dr. J.D. Rozich, Luther Midelfort, Mayo Health System, Eau Claire, WI 54703, United States. rozich.john@mayo.edu
SOURCE: Quality and Safety in Health Care, (2003) 12/3 (194-200). Refs: 16
ISSN: 0963-8172 CODEN: QSHCA5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Adverse drug events continue to be the single most frequent source of healthcare mishaps, continually placing patients at **risk** of injury. This is not unexpected, given that drug treatment is the most common medical intervention and medication use is a highly complex, multidisciplinary, and largely manual process. Assessing the actual safety of drug use has been historically difficult, mainly because traditional **methods** such as chart audits and voluntary reporting of data have been shown to be expensive, insensitive, and largely ineffective for detecting mistakes in **drug administration** and drug related adverse clinical events (ADEs). Computerized **methods** for detecting ADEs, employing sentinel words or "triggers" in a patient's medical record, are effective but expensive and require customized software linkage to pharmacy databases. This paper describes the use of the "trigger tool", a relatively low cost and "low tech" modification of the automated technique. The adapted technique appears to increase the rate of ADE detection approximately 50-fold over traditional reporting **methodologies.**

L30 ANSWER 12 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002415202 EMBASE
TITLE: [**Clostridium difficile** infection in a Department of Internal Medicine. A consecutive series of 45 patients].
L'INFECTION A **CLOSTRIDIUM DIFFICILE**: DANS UN SERVICE DE MEDECINE INTERNE A PROPOS D'UNE SERIE

CONSECUTIVE DE 45 PATIENTS.
AUTHOR: Bligny D.; Cador B.; Jolivet-Gougeon A.; Le Strat A.; Cazalets C.; Laurat E.; Jego P.; Bouget J.; Grosbois B.
CORPORATE SOURCE: B. Grosbois, Departement de Medecine Interne, CHU Hopital Sud, 16, boulevard de Bulgarie, 35056 Rennes Cedex, France. bernard.grosbois@chu-rennes.fr
SOURCE: Annales de Medecine Interne, (2002) 153/5 (291-299).
Refs: 44
ISSN: 0003-410X CODEN: AMDIBO
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
006 Internal Medicine
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: French
SUMMARY LANGUAGE: English; French
AB Objective and **methods.** - A retrospective study of 45 patients with **Clostridium difficile** infection over a 4-year period in a department of Internal Medicine. Results. - Mean age was 79 years; sex-ratio (F/M) = 1.5; 38% of the patients had neurological or severe psychiatric disorders; 20% had a neoplastic disease. Ninety-three percent of cases had received one or more antibiotics before onset of **diarrhea**, prescribed mainly for a pulmonary infection. Amoxicillin ± clavulanic acid and cephalosporins were the most frequently used treatments, respectively in 48% and 40% of cases. For 25 patients (56%) **Clostridium difficile**-associated **diarrhea** was considered as a nosocomial infection, and as community-acquired **diarrhea** in 20 cases (44%). Treatment included isolation of the patient as soon as bacteriological diagnosis was known and specific therapy was instituted by metronidazole or vancomycin for a mean of 18 days. The addition of Saccharomyces boulardii was used in of cases. The clinical course was rapidly favorable for 80% of patients. Five patients died with complications of severe colitis in 2 cases. Mean hospital stay was 49 days (annual mean of the department = 10 days). Conclusion. - **Clostridium difficile diarrhea** concerns above all elderly patients with one or more underlying pathologies. Amoxicillin ± clavulanic acid and third-generation cephalosporins are the most frequently prescribed antibiotics in these cases and have the highest correlation with this infectious complication. This medical problem requires greater knowledge as it causes significant morbidity and increases the **risk** of prolonged hospital stays.

L30 ANSWER 13 OF 26 EMBASE
on STN
ACCESSION NUMBER: 2002183294 EMBASE
TITLE: Clinical significance of the emergence of bacterial resistance in the hospital environment.
AUTHOR: Hosein I.K.; Hill D.W.; Jenkins L.E.; Magee J.T.
CORPORATE SOURCE: Dr. I.K. Hosein, Cardiff Public Health Laboratory, University Hospital of Wales, Heath Park, Cardiff CF14 4XW, United Kingdom
SOURCE: Journal of Applied Microbiology Symposium Supplement, (2002) 92/1 (90S-97S).
Refs: 57
ISSN: 0267-4440 CODEN: SAPBB7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology

037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Antibiotic resistance is an increasing threat in hospitals and both morbidity and mortality from infections are greater when caused by drug-resistant organisms. Whilst hospitals are universally blamed for this increase, there is an insufficient appreciation of external sources of resistance, such as when patients are admitted to hospitals from long-term care facilities in the community. The use of antibiotics in family practice and animal husbandry has also been linked to drug resistance being encountered in the hospital setting. Justifiable hospital antibiotic use, which can be life saving, may lead to 'collateral damage' with the emergence of resistance in non-target bacteria in the bowel, for example, with subsequent spread by cross-infection. At a management level, antibiotic resistance can have a significant impact on the ability of hospitals to maintain services since cohorting of patients and ward closures from outbreaks add to continuing bed shortages and waiting lists. Hospital laboratories must review their standard operating procedures since some resistance mechanisms may be missed by current **methods** of antibiotic susceptibility testing. With increasing public concern from press reports of 'multiresistant Staphylococcus aureus killer virus' and other drug-resistant organisms, there will inevitably be a push by national authorities for more surveillance data on antibiotic resistance; however, the cost-effectiveness of different surveillance strategies should be considered. Clinical governance and **risk** management are dominant themes in the National Health Service and hospital hygiene and antibiotic resistance are likely to feature prominently in audits related to these themes in the near future.

L30 ANSWER 14 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001241496 EMBASE
TITLE: Decompressive colonoscopy with intracolonic vancomycin administration for the treatment of severe pseudomembranous colitis.
AUTHOR: Shetler K.; Nieuwenhuis R.; Wren S.M.; Triadafilopoulos G.
CORPORATE SOURCE: G. Triadafilopoulos, Section of Gastroenterology, Gastroenterology Division, Stanford Univ. School of Medicine, Stanford, CA, United States
SOURCE: Surgical Endoscopy, (2001) 15/7 (653-659).
Refs: 34
ISSN: 0930-2794 CODEN: SUREEX
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 009 Surgery
014 Radiology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: We explored the potential of early decompressive colonoscopy with intracolonic vancomycin administration as an adjunctive therapy for severe pseudomembranous **Clostridium difficile** colitis with ileus and toxic megacolon. **Methods**: We reviewed the symptoms, signs, laboratory tests, radiographic findings, and outcomes from the medical records of seven patients who experienced eight episodes of severe pseudomembranous colitis with ileus and toxic megacolon. All seven patients underwent decompressive colonoscopy with intracolonic perfusion of vancomycin. Results: Fever, abdominal pain, **diarrhea** , abdominal distention, and tenderness were present in all patients. Five

of seven patients were comatose, obtunded, or confused, and six of the seven required ventilatory support. The white blood cell count was greater than 16,000 in seven cases (six patients). Colonoscopy showed left-side pseudomembranous colitis in one patient, right-side colitis in one patient, and diffuse pseudomembranous pancolitis in five patients. Two patients were discharged with improvement. Five patients had numerous medical problems leading to their death. Complete resolution of pseudomembranous colitis occurred in four patients. One patient had a partial response, and two patients failed therapy. Conclusion: Colonoscopic decompression and intracolonic vancomycin administration in the management of severe, acute, pseudomembranous colitis associated with ileus and toxic megacolon is feasible, safe, and effective in approximately 57% to 71% of cases.

L30 ANSWER 15 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001124711 EMBASE
TITLE: **Clostridium difficile** infection: **Risk** factors, medical and surgical management.
AUTHOR: Klingler P.J.; Metzger P.P.; Seelig M.H.; Pettit P.D.M.; Knudsen J.M.; Alvarez S.
CORPORATE SOURCE: Dr. S. Alvarez, Department of Infectious Diseases, Mayo Clinic, 4500 San Pablo Road, Jacksonville, FL 32224, United States. salvarez@mayo.edu
SOURCE: Digestive Diseases, (2000) 18/3 (147-160).
Refs: 190
ISSN: 0257-2753 CODEN: DIDIEW
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background: **Clostridium difficile** has become recognized as a cause of nosocomial infection which may progress to a fulminant disease. **Methods**: Literature review using electronic literature research back to 1966 utilizing Medline and Current Contents. All publications on antibiotic-associated **diarrhea**, antibiotic-associated colitis, and pseudomembranous colitis as well as C. difficile infection were included. We addressed established and potential **risk** factors for C. difficile disease such as an impaired immune system and cost benefits of different diagnostic tests. An algorithm is outlined for diagnosis and both medical and surgical management of mild, moderate and severe C. difficile disease. Results: Diagnosis of C. difficile infection should be suspected in patients with **diarrhea** , who have received antibiotics within 2 months or whose symptoms started after hospitalization. A stool specimen should be tested for the presence of leukocytes and C. difficile toxins. If this is negative and symptoms persist, stool should be tested with 'rapid' enzyme immunoabsorbent and stool cytotoxin assays, which are the most cost-effective tests. Endoscopy and other imaging studies are reserved for severe and rapidly progressive courses. Oral metronidazole or vancomycin are the antibiotics of choice. Surgery is rarely required for selected patients refractory to medical treatment. The threshold for surgery in severe cases with **risk** factors including an impaired immune system should be low. Conclusion: C. difficile infection has been recognized with increased frequency as a nosocomial infection. Early diagnosis with immunoassays of the stool and

prompt medical therapy have a high cure rate. Metronidazole has supplanted oral vancomycin as the drug of first choice for treating C. difficile infections. Copyright .COPYRGT. 2000 S. Karger AG, Basel.

L30 ANSWER 16 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000188457 EMBASE
TITLE: **Clostridium difficile**-associated diarrhoea in hospitalised patients.
AUTHOR: Al-Eidan F.A.; McElnay J.C.; Scott M.G.; Kearney M.P.
CORPORATE SOURCE: Prof. J.C. McElnay, Pharmacy Practice Research Group, The School of Pharmacy, The Queen's University of Belfast, 97 Lisburn Road, Belfast BT9 7BL, United Kingdom.
j.mcelnay@qub.ac.uk
SOURCE: Journal of Clinical Pharmacy and Therapeutics, (2000) 25/2 (101-109).
Refs: 48
ISSN: 0269-4727 CODEN: JCPTED
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objective: The aim of the present study was to evaluate the incidence, **risk** factors and cost implications of **Clostridium difficile**-associated diarrhoea (CDAD) in hospitalized adult patients. **Methods**: Eighty-seven hospitalized adult patients, positively identified as having CDAD, were reviewed retrospectively to determine the **risk** factors and cost implications of CDAD. Results: The clinical manifestations, in addition to diarrhoea, included elevated temperature (= 37.8°C; 42.5%), abdominal pain (63.2%) and leucocytosis (= 12 x 109 cells/l; 52.9%). Eight patients underwent endoscopy, and pseudomembranous colitis was confirmed in all of these patients. Nine patients died during their hospital stay. Cefotaxime and cefuroxime were the agents most commonly associated with CDAD. There was a significant difference ($P < 0.001$) between the sex distribution of CDAD patients and adult hospital patients (69% of CDAD patients were female vs. 52% of general adult hospital population). Significantly ($P < 0.001$) more patients with CDAD were admitted from the nursing home (NH) setting. The mean age of patients with CDAD admitted from NHs ($n = 19$) was older than those cases admitted from the community ($n = 68$) by 14 years ($P < 0.001$). The length of hospital stay was significantly ($P < 0.001$) longer for patients with CDAD (16.9 vs. 3.89 days). No differences ($P = 0.306$) were found in the response times for CDAD patients treated with either oral metronidazole ($n = 39$) or oral vancomycin ($n = 48$). The mean response time was, however, significantly longer in the CDAD patients admitted from NHs (4.2 days) compared with those admitted from the community (2.5 days), although the former patients were older and had significantly more comorbidity ($P < 0.001$). The mean cost per one treated-case of CDAD (bed, laboratory requests and treatment therapy) was calculated as £2860. Conclusions: Patients admitted from NHs are at increased **risk** of development of CDAD; receiving cefotaxime or cefuroxime axetil (oral form), being elderly and being female are **risk** factors for the development of CDAD. Treatment of CDAD with oral metronidazole or oral vancomycin gives rise to similar response times and efficacy.

L30 ANSWER 17 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999397659 EMBASE

TITLE: An antibiotic policy associated with reduced **risk** of **Clostridium difficile**-associated diarrhoea.

AUTHOR: Ludlam H.; Brown N.; Sule O.; Redpath C.; Coni N.; Owen G.

CORPORATE SOURCE: H. Ludlam, Microbiol. Public Health Laboratory, Addenbrooke's Hospital, Cambridge CB2 2QW, United Kingdom. hugo.ludlam@msexc.addenbrookes.anglox.nhs.uk

SOURCE: Age and Ageing, (1999) 28/6 (578-580).
Refs: 5
ISSN: 0002-0729 CODEN: AANGAH

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
020 Gerontology and Geriatrics
036 Health Policy, Economics and Management
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Background: antibiotic-associated diarrhoea caused by **Clostridium difficile** is increasing in hospitals, and older people are at particular **risk.** Objective: to establish whether reducing patient exposure to injectable third-generation cephalosporins by substituting alternative antibiotics can produce a cost-effective reduction in the incidence of antibiotic-associated diarrhoea. Design: we prospectively investigated 2157 patients admitted to the department of elderly medicine in the year before introduction of antibiotic restrictions and 2037 patients admitted in the following year. Patients admitted to other wards, where antibiotic prescribing was unchanged, acted as controls. Setting: a 900-bed teaching hospital in Cambridge, UK. Measurements: use and cost of injectable antibiotics prescribed in the department of elderly medicine and the other wards studied; occurrence of C. difficile-associated diarrhoea. Results: in the wards for older people, consumption of injectable cephalosporins fell by 92% (compared with 8% on other wards) and cases of C. difficile-associated diarrhoea fell from 98 to 45 (cases in other wards rose from 213 to 253; $P < 0.001$). The £8062 increase in injectable antibiotic costs on the elderly wards were offset by the release of 1087 wasted bed-days attributable to the 53 fewer cases, with potential savings of £212,000. Conclusions: restricting the consumption of injectable third-generation cephalosporins is a cost-effective **method** of reducing the incidence of C. difficile-associated diarrhoea.

L30 ANSWER 18 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1998423262 EMBASE

TITLE: Prospective study of the **risk** of **Clostridium difficile** diarrhoea in elderly patients following treatment with cefotaxime or piperacillin-tazobactam.

AUTHOR: Settle C.D.; Wilcox M.H.; Fawley W.N.; Corrado O.J.; Hawkey P.M.

CORPORATE SOURCE: Dr. M.H. Wilcox, The General Infirmary at Leeds, Old Medical School, Leeds LS1 3EX, United Kingdom. markwi@pathology.leeds.ac.uk

SOURCE: Alimentary Pharmacology and Therapeutics, (1998) 12/12 (1217-1223).
Refs: 23

ISSN: 0269-2813 CODEN: APTHEN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: Rates of **Clostridium difficile** diarrhoea have recently been rising, with the elderly being at highest **risk**. Aim: To compare the incidence of C. difficile colonization and diarrhoea in elderly patients treated for presumed infection with either empirical cefotaxime (CTX) or piperacillin-tazobactam (PT). **Methods**: A prospective, ward-based, crossover study was carried out on two well-matched care of the elderly wards at a UK tertiary care hospital, in patients requiring empirical broad-spectrum antibiotic treatment. Results: There was a highly significant increased incidence of C. difficile colonization (26/34 vs. 3/14, P = 0.001) and diarrhoea (18/34 vs. 1/14, P = 0.006) in patients who received CTX as opposed to PT. DNA fingerprinting suggested that most infections arose from strains acquired from the hospital environment. Conclusions: Elderly patients are significantly less likely to develop C. difficile diarrhoea after treatment with PT than after CTX. The source of C. difficile appears to be predominantly from the ward environment.

L30 ANSWER 19 OF 26 EMBASE
on STN
ACCESSION NUMBER: 1998204375 EMBASE
TITLE: Case-controlled review of **Clostridium difficile**-associated diarrhoea in Southern Tasmania.
AUTHOR: Halim H.A.; Peterson G.M.; Friesen W.T.; Ott A.K.
CORPORATE SOURCE: G.M. Peterson, Tasmanian School of Pharmacy, Faculty of Medicine and Pharmacy, University of Tasmania, GPO Box 252-26, Hobart, Tasmania 7001, Australia
SOURCE: Journal of Clinical Pharmacy and Therapeutics, (1997) 22/5-6 (391-397).
Refs: 27
ISSN: 0269-4727 CODEN: JCPTED
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Aim: While the incidence of **Clostridium difficile** associated diarrhoea (CDAD) has increased sharply over the last 15 years, its **risk** factors are still not well defined. The aim of this study was to review cases of CDAD at the major teaching hospital in Tasmania, Australia, to identify **risk** factors for CDAD and their association with prognosis. **Methods**: A retrospective review of the medical records of adult patients admitted to the hospital between January 1994 and December 1996 was performed. Sixty-four patients who developed CDAD prior to or during their admission, and an additional 120 diarrhoea-free patients (the control group) were studied. An extensive range of demographic and clinical variables were recorded, and the differences between the control group and patients with CDAD were

evaluated. Results: The CDAD patients had a median age of 66 years (range 22-95 years), with females accounting for 52% of cases. There were no significant demographic differences from the control group. Identifiable **risk** factors for developing CDAD were severe underlying disease, renal impairment, exposure to antibiotics or antineoplastic agents, and the use of total parenteral nutrition or nasogastric feeding. Cephalosporins were the most frequently used antibiotics in both CDAD and control patients, with cefotaxime being the only antibiotic which was identified as being significantly associated with an increased **risk** of CDAD. The median length of diarrhoea episodes was 9 days (range 1-60 days). The mortality rate was 17.2%, and factors associated with a poor prognosis were older age, severe underlying disease, renal impairment and failure to treat with metronidazole or vancomycin. Delay in starting specific treatment and use of codeine were related to prolonged CDAD. Conclusion: CDAD is a growing contributor to hospital morbidity and costs. Severely ill patients with compromised immune function are particularly susceptible, with antibiotic use being a major **risk** factor. Prompt diagnosis and initiation of treatment are important factors in the improvement of prognosis.

L30 ANSWER 20 OF 26 EMBASE
on STN

ACCESSION NUMBER: 1998158133 EMBASE

TITLE: [**Clostridium difficile**-associated diarrhoea in paediatric patients - Incidence, therapeutic indications, and treatment strategy].
CLOSTRIDIUM-DIFFICILE-ASSOZIIERTE DIARRHOE BEI PADIATRISCHEN PATIENTEN - VORKOMMEN, THERAPIEINDIKATIONEN UND BEHANDLUNGSSTRATEGIE.

AUTHOR: Simon A.; Fleischhack G.; Hasan C.; Marklein G.; Bode U.

CORPORATE SOURCE: Dr. A. Simon, Abteilung Hamatologie/Onkologie, Zentrum fur Kinderheilkunde, Adenauerallee 119, 53113 Bonn, Germany

SOURCE: Hygiene + Medizin, (1998) 23/4 (109-114).
Refs: 44
ISSN: 0172-3790 CODEN: HYMEDG

COUNTRY: Germany

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 004 Microbiology
007 Pediatrics and Pediatric Surgery
037 Drug Literature Index
048 Gastroenterology

LANGUAGE: German

SUMMARY LANGUAGE: English; German

AB Pseudo-membranous colitis caused by **Clostridium difficile** has been described as a serious complication of antibiotic therapy which also affects paediatric patients. The symptomatic form of the disease is rare in neonates and infants, even though up to 60% of all children at this age temporarily carry toxin-producing **Clostridium difficile.** Colonisation of paediatric patients is usually a result of nosocomial transmission e.g. on neonatological wards or of clostridia pandemics in day-care centres and kindergartens. The most important **risk** factors for symptomatic **Clostridium difficile** infection are antibiotic pretreatment (especially with cephalosporine), long-term hospitalisation, poor general health, advanced renal failure, diabetes mellitus, or long-term administration of glucocorticoids. Strict adherence to basic infection control measures in the hospital (single-use gloves, patient-related gown management, hand disinfection, routine scrub disinfection of the inanimate environment, if possible physical seclusion of carriers) for the duration of the disease cannot prevent the spread of

clostridia in all cases, since bacterial spores are not completely inactivated in all cases. The recurrence rate is 55% even following successful treatment, and as yet there are no effective **methods** for treating asymptomatic carriers. Available data suggest a clinically oriented treatment strategy for symptomatic patients who tested positive for toxins. In those recurrences so frequently seen this strategy is employed in the same manner. All antibiotic therapy should be discontinued if at all possible. Patients in generally stable condition in whom the symptoms do not subside after this measure are treated with metronidazole administered orally or intravenously. Intravenous administration is particularly advantageous in oncological patients suffering from severe mucositis or intestinal obstruction. Vancomycin should be kept in reserve and be restricted to severe cases with gravely deteriorated overall patient health or with very pronounced pseudo-membranous colitis, and should always be given orally (e.g. by gastric intubation). In rare cases, additional rectal or caecal administration of the vancomycin solution may be indicated. In acute abdominal disease, protracted severe progression, or exacerbation despite appropriate therapy, paediatric surgeons should be included in the medical team at an early stage.

L30 ANSWER 21 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1998123722 EMBASE
TITLE: Metronidazole may inhibit intestinal colonization with **Clostridium difficile.**
AUTHOR: Cleary R.K.; Grossmann R.; Fernandez F.B.; Stull T.S.; Fowler J.J.; Walters M.R.; Lampman R.M.
CORPORATE SOURCE: Dr. R.K. Cleary, St. Joseph Mercy Hospital, 5333 McAuley Drive, Ann Arbor, MI 48106, United States
SOURCE: Diseases of the Colon and Rectum, (1998) 41/4 (464-467). Refs: 20
ISSN: 0012-3706 CODEN: DICRAG
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
009 Surgery
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB PURPOSE: Antibiotics suppress normal gut flora, allowing overgrowth of acquired or native **Clostridium difficile**, with release of toxins that cause mucosal inflammation. Oral metronidazole is used to treat antibiotic- associated colitis (pseudomembranous colitis). This study was designed to determine whether oral metronidazole, as part of preoperative bowel preparation, prevents or decreases incidence of antibiotic-associated colitis after elective colonic and rectal procedures. **METHODS**: Eighty-two patients (40 men) were prospectively, randomly assigned to receive one of two oral antibiotic regimens before colorectal surgery. All patients underwent mechanical bowel preparation with polyethylene glycol-electrolyte lavage solution before administration of oral antibiotics. Group 1 (n = 42) patients received three doses (1 g/dose) of neomycin and erythromycin. Group 2 (n = 40) patients received three doses (1 g/dose) of neomycin and metronidazole. Both groups received one preoperative and three postoperative doses of intravenous cefotetan (2 g/dose). Both groups had stool samples tested for C difficile toxin in the preoperative and postoperative periods by enzyme- linked immunoabsorbent assay or by tissue culture cytotoxicity. Patients with preoperative stool studies positive for C difficile were excluded from the study. RESULTS: Treatment groups

were not different for age, gender, or surgical procedure. Mean age ± 1 standard deviation was 67.6 ± 13.6 (range, 34-94) years in Group 1 and 62.1 ± 13.5 (range, 35-84) years in Group 2 (P = 0.069). Mean length of hospital stay ± 1 standard deviation was 9.76 ± 4.9 (range, 4-28) days for Group 1 and 8.05 ± 2.6 (range, 3-14) days for Group 2 (P = 0.053). Five patients in Group 1 (neomycin and erythromycin) and one patient in Group 2 (neomycin and metronidazole) had positive stool studies for C difficile. Relative **risk** of colonization with C. difficile in Group 1 was 4.76 times that in Group 2 (95 percent confidence interval, 0.581, 39). This difference was not statistically significant (P = 0.202). There were no significant differences in C difficile colonization rates with respect to age, length of stay, or gender. CONCLUSIONS: This study suggests that there may be a clinical association between use of metronidazole preoperatively and inhibition of intestinal colonization by C difficile in this patient population undergoing colonic and rectal surgery.

L30 ANSWER 22 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 96095778 EMBASE
DOCUMENT NUMBER: 1996095778
TITLE: **Risk** of diarrhoea due to **Clostridium difficile** during cefotaxime treatment [9].
AUTHOR: ✓ Rothschild E.; Rauss A.; Danan G.; Lesna M.; Parham D.M.; Impallomeni M.; Starr J.; Rogers T.
CORPORATE SOURCE: Corporate Drug Safety Epidemiol Dept, Roussel Uclaf, 102 Route de Noisy,93235 Romainville, France
SOURCE: British Medical Journal, (1996) 312/7033 (778).
ISSN: 0959-8146 CODEN: BMJOAE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 004 Microbiology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English

L30 ANSWER 23 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 95196069 EMBASE
DOCUMENT NUMBER: 1995196069
TITLE: The challenge of vancomycin-resistant enterococci: A clinical and epidemiologic study.
AUTHOR: Lam S.; Singer C.; Tucci V.; Morthland V.H.; Pfaller M.A.; Isenberg H.D.
CORPORATE SOURCE: Long Island Jewish Medical Center, 270-05 76th Ave.,New Hyde Park, NY 11040, United States
SOURCE: American Journal of Infection Control, (1995) 23/3 (170-180).
ISSN: 0196-6553 CODEN: AJICDC
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background: Vancomycin-resistant enterococci have been recovered with increasing frequency from hospitalized patients. **Risk** factors,

mode of nosocomial transmission, extent of colonization in hospitalized patients, and treatment options for these organisms have not been completely delineated. **Methods**: We studied 53 patients (group A) with vancomycin-resistant enterococci isolated from various clinical specimens and also surveyed for vancomycin-resistant enterococci in stool specimens submitted for **Clostridium difficile** toxin assays (group B). Stool specimens submitted for identification of bacterial pathogens and stool specimens from hospital employees were also analyzed for vancomycin-resistant enterococci. Results: Seventy-six isolates of vancomycin-resistant enterococci were recovered in group A. Five of these patients harbored vancomycin-resistant enterococci on admission. Fifty-three of 289 group B stool specimens submitted for C. difficile toxin assays yielded vancomycin-resistant enterococci. Cephalosporins and vancomycin were the most common antimicrobial agents received by both groups of patients. Enterococcus faecium isolates were more resistant than Enterococcus faecalis isolates to antimicrobial agents. All isolates exhibited high level aminoglycoside resistance and were not β- lactamase producers. There were at least 15 different molecular clones of E. faecium and three of E. faecalis. Vancomycin resistant enterococcal bacteremia was associated with a 100% in hospital mortality rate. Conclusions: Multidrug-resistant and vancomycin-resistant enterococci have become important nosocomial pathogens that are difficult to treat. Vancomycin-resistant enterococcal bacteremia was associated with a poor prognosis. We found a high rate of colonization in patients with suspected C. difficile toxin colitis. Judicious use of vancomycin and broad-spectrum antibiotics is recommended, and strict infection control measures must be implemented to prevent nosocomial transmission of these organisms.

L30 ANSWER 24 OF 26 EMBASE
on STN

ACCESSION NUMBER: 94252551 EMBASE
DOCUMENT NUMBER: 1994252551
TITLE: **Clostridium difficile**-associated **diarrhea** in patients with HIV positivity and AIDS: A prospective controlled study.
AUTHOR: Sain Sain Lu; Schwartz J.M.; Simon D.M.; Brandt L.J.
CORPORATE SOURCE: Division of Gastroenterology, Department of Medicine, Montefiore Medical Center, 111 East 210th Street,Bronx, NY 10467, United States
SOURCE: American Journal of Gastroenterology, (1994) 89/8 (1226-1229).
ISSN: 0002-9270 CODEN: AJGAAR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objective: To compare the clinical manifestations and therapeutic responses of **Clostridium difficile** infection in HIV-infected and noninfected individuals. **Methods**: Patients were identified for this study if they had C. difficile toxin in the stool. The patients were then followed prospectively by the investigators. All patients were treated with a standard regimen, and clinical and laboratory findings were recorded. Persistence and resolution or recurrence of symptoms and complications were recorded. Results: A total of 87 patients were studied, of which 12 were HIV positive, 20 had AIDS, and 55 had no known HIV infection. The AIDS group was younger and had a lower total

leukocyte count than the controls. There were no statistically significant differences in temperature, leukocytosis, clinical symptoms, therapeutic response, or recurrence or persistent of symptoms. Conclusions: Despite the immunosuppression of HIV infection, C. difficile infection behaves no differently in HIV/AIDS patients than it does in controls.

L30 ANSWER 25 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 85122075 EMBASE
DOCUMENT NUMBER: 1985122075
TITLE: Effect of therapy with latamoxef (moxalactam) on carriage of **Clostridium difficile.**
AUTHOR: Deery H.G.; Jones P.G.; Kauffman C.A.; et al.
CORPORATE SOURCE: Division of Infectious Diseases, Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, MI, United States
SOURCE: Journal of Antimicrobial Chemotherapy, (1984) 13/5 (521-524).
CODEN: JACHDX
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
004 Microbiology
LANGUAGE: English
AB Twenty-seven patients receiving latamoxef (moxalactam) as a single antimicrobial agent were studied prospectively for **Clostridium difficile** carriage and development of diarrhoea or colitis. Stools were available prior to therapy from only 7 patients, one of whom (14.3%) was an asymptomatic carrier. None of 12 patients studied during therapy were carriers. Seven of 27 patients (25.9%) were colonized with Cl. difficile after completion of latamoxef therapy, and 3 patients had cytotoxin positive stools. Two patients with cytotoxin grew Cl. difficile from stools and 1 patient was culture negative. Only 1 patient, who had both culture and cytotoxin positive stools, had profuse diarrhoea. Cl. difficile clinical isolates were only moderately susceptible to latamoxef in vitro. Hamsters given moxalactam developed caecitis. Patients receiving latamoxef, or third generation cephalosporins, may be at increased **risk** of development of Cl. difficile associated diarrhoea and should be followed closely for this complication, especially after therapy has been discontinued.

L30 ANSWER 26 OF 26 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-300892 [29] WPIDS
DOC. NO. CPI: C2003-078539
TITLE: Producing immune stimulating agent, by cultivating Lentinus edodes in liquid growth medium for extracellular accumulation of immune stimulating agent, and isolating extracellularly located immune stimulating agent.
DERWENT CLASS: B04 D16
INVENTOR(S): KRISTIANSEN, B
PATENT ASSIGNEE(S): (MEDI-N) MEDIMUSH APS
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003020944	A2	20030313	(200329)*	EN	29

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003020944	A2	WO 2002-IB3557	20020903

PRIORITY APPLN. INFO: NO 2001-4256 20010903

AN 2003-300892 [29] WPIDS

AB WO2003020944 A UPAB: 20030505

NOVELTY - Producing (M) an immune stimulating agent comprising cultivating a fungus of the genus Lentinus in a liquid growth medium (LGM), where the cultivation results in extracellular accumulation of the immune stimulating agent, and isolating the extracellularly located immune stimulating agent from the liquid growth medium, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an immune stimulating agent (I) obtainable from the extracellular part of LGM;

(2) a pharmaceutical composition (PC) comprising (I) and a carrier; and

(3) a pharmaceutical kit comprising PC in solid form and a dosage regime instruction with guidelines for dose and times for administration.

ACTIVITY - Antiparasitic; Antibacterial; Antiinflammatory; Neuroprotective; Virucide; Antidiarrheic; Hepatotropic; Tuberculostatic; Immunosuppressive; Anti-HIV; Fungicide.

MECHANISM OF ACTION - Stimulator of immune response (claimed).

12 weeks old Sprague Dawley rats were given 1 mg of intracellular or extracellular lentinan in 0.5 ml 0.09 saline (i.p.) 2 days before the **immunization.** Control animals received 1 mg casein. The animals were **immunized** with bovine serum albumin (BSA) (0.5 mg) in 0.25 Freunds Complete Adjuvant and blood samples were obtained after 11 days for measurement of the antibody response. The specific anti-BSA antibody concentration was determined against an absolute standard of antibody BSA by sandwich ELISA. The anti-BSA Ig production in control, cellular lentinan, and extracellular lentian treated animal was 9, 16, and 26 mu g/ml of serum, respectively. This immunological experiment demonstrated that lentinan was an active stimulator of immune system. The extracellular product provided a higher response than intracellular lentinan.

USE - (M) is useful for producing an immune stimulating agent. PC is useful for treating an individual diagnosed with an immune compromised condition, for treating an individual at **risk** of contracting an immune compromised condition, for treating an individual recovering from surgery or illness and at **risk** of contracting an immune compromised condition, and for treatment an individual diagnosed with or at **risk** of contracting acquired immunodeficiency syndrome. The individual is a mammal including a **human** being. The immune compromised condition is an infectious disease, parasitic disease, Haemophilus meningitis, pneumococcal meningitis, streptococcal meningitis, staphylococcal meningitis, meningitis due to other organisms, encephalitis, viral pneumonia, pneumococcal pneumonia, other bacterial pneumonia, pneumonia due to other specified organisms except bacteria, bronchopneumonia, organism unspecific pneumonia, influenza, unspecified **diarrhea**, hepatitis unspecified, acute and subacute necrosis of the liver, chronic hepatitis, and abscess of liver. The immune compromised

condition is an infectious or parasitic disease caused by or selected from cholera, Salmonella, shigellosis, Escherichia coli, intestinal infection due to other specified bacteria, **Clostridium difficile** , viral gastroenteritis, infectious colitis, enteritis and gastroenteritis, infectious **diarrhea**, tuberculosis, listeriosis, pasteurellosis, Mycobacterium, diphtheria, pertussis, meningococcus, Streptococcus septicaemia, Staphylococcus septicaemia, pneumococcal septicaemia, septicaemia due to anaerobes, septicaemia due to other gram-negative organisms, actinomycotic infection, gas gangrene, toxic shock syndrome, necrotizing faciitis, Friedlander's bacillus, Haemophilus influenzae, Pseudomonas, AIDS/HIV infections, acute poliomyelitis, Creutzfeldt-Jacob disease, subacute sclerosing panencephalitis, progressive multifocal leucoencephalopathy, unspecified slow virus infection of central nervous system, coxsackie virus, unspecified viral meningitis, lymphocytic choriomeningitis, unspecified viral encephalitis, chickenpox, Herpes zoster, Herpes simplex, viral hepatitis A, viral hepatitis B, other specified viral hepatitis, chronic hepatitis, abscess/acute necrosis of liver, infectious mononucleosis, cytomegalic inclusion disease, chlamydiae, adenovirus, viral infection, syphilis, Candida, unspecified histoplasmosis, aspergillosis, cryptococcosis, mycoses, strongyloidiasis, intestinal parasitism, toxoplasmosis, sarcoidosis, Pneumocystis carinii, post polio syndrome, Haemophilus meningitis, Pneumococcal meningitis, Streptococcal meningitis, Staphylococcal meningitis, encephalitis, pneumonia due to adenovirus, pneumonia due to respiratory syncytial virus, pneumonia due to parainfluenza virus, pneumonia due to other virus, viral pneumonia, pneumococcal pneumonia, pneumonia due to Klebsiella pneumoniae, Pseudomonas, Haemophilus influenzae, Streptococcus, or Staphylococcus, and bacterial pneumonia. PC is useful in the manufacture of a medicament for treatment of an immune compromised condition of an individual in need of such treatment. The treatment is prophylactic, ameliorating or curative. Dwg.0/0